(a) [a DNA molecule obtainable from] screening a human recombinant cDNA library [or genomic DNA library] prepared from tissue expressing human TNF-R2 at a detectable level [(a) by the yeast two-hybrid technique or (b) by cross-species hybridization] with [an] one or more labeled oligonucleotide [sequence] probe(s) having about 30 to 50 bases derived from the nucleotide sequence encoding murine TRAF1 (SEQ. ID. NO:1) [and] or murine TRAF2 (SEQ. ID. NO:3) , wherein said probe(s) are designed based on TRAF1 or TRAF2 regions which have the least codon redundance, under stringent conditions comprising overnight incubation at 42 °C in a solution comprising 20% formamide, 5xSSC, 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 g/ml denature, sheared salmon sperm DNA;

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(b) inserting the DNA hybridizing to said probe(s) into a replicable expression vector;

(c) transforming a recombinant host cell with said expression vector;

(d) culturing the transformed host cell; and

(e) recovering said human TRAF .

[Please amend claim 32 as follows:]

2 ~~32.~~ (Amended) [An] The isolated human [tumor necrosis factor receptor associated factor ()TRAF[)] of claim ~~31~~ 1, wherein said oligonucleotide probes are derived from the nucleotide sequence encoding murine TRAF1 (SEQ. ID. NO: 1) [which is the human homolog of murine TNFR1 (SEQ. ID. NO: 2)].

[Please amend claim 33 as follows:]

3 ~~33.~~ (Amended) [An] The isolated human [tumor necrosis factor receptor associated factor ()TRAF[)] of claim ~~31~~ 1, wherein said oligonucleotide probes are derived from the nucleotide sequence encoding murine TRAF2 (SEQ. ID. NO: 3 [which is the human homolog of the murine TNFR2 (SEQ. ID. NO: 4)].

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Support for the Amendments

Support for the amendments in the claims is at least at page 20, lines 21-24; page 33, lines 13-26; page 34, lines 10-14; and page 36, lines 9-19.

The Rejections

(1) Applicants were requested to delete from the first sentence of this application the incorporation by reference of application Serial No. 08/250,858. The foregoing amendment in the specification is believed to comply with the requirement.

(2) Claims 31 to 33 were rejected under 35 U.S.C. 112, first paragraph for alleged lack of enablement. The Examiner noted that the present application "does not describe even a single protein of human origin which meets the limitations of the instant claims", and suggested that since the "TNF receptors are not structurally and functionally conserved between mammalian species an artisan would not reasonably expect the proteins associated therewith to be conserved between mice and humans."

The claims as presently amended define the human TRAF protein by the process by which it is obtained. All steps of the process are specifically disclosed in the specification and are well known in the art, accordingly, can be performed without undue experimentation. The Examiner's suggestion that a high degree of sequence identity was not to be expected between the murine and human TRAF proteins is believed to be irrelevant for the question of enablement. The present application specifically teaches that human homologs of the murine TRAF proteins can be obtained by cross-species hybridization and subsequent expression. Indeed, the murine and human TRAF proteins show an 86% overall sequence identity (Mosialos et al., of record). Since the present inventors had the foresight to anticipate and teach this result, they are entitled to claim the product of cross-species hybridization. The fact that others might not have expected

a high degree of sequence identity between murine and human TRAF proteins only underscores the unobviousness of the invention claimed in the present application, and should, therefore, be viewed as a factor further supporting patentability.

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(3) Claims 31 to 33 were rejected as "vague and indefinite" in their use of the phrase "obtainable". In addition, claims 32 and 33 were rejected since the reference to "the" human homolog, had not antecedent basis. Claim 31 was rejected as vague, since it did not recite the hybridization conditions, and referred an oligonucleotide "sequence" as hybridizing. The foregoing amendments are believed to overcome these rejections, the withdrawal of which is respectfully requested.

The present application is believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Respectfully submitted,
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